Pathology is the study of disease producing constellations and their effect on living organisms. It has reared itself since the time of Virchow to the status of a science, if any field in biology may be truly called a science, and as such has and can divorce itself from its previous service position as the hand maid of medicine.; yet, for us its greatest raison distre is the part it plays in elucidating the processes of disease in man. It is well to remember from the very beginning however that the purpose of any science is to reconstruct physical experience into a system of law and order,; to bring natural phenomena closer to our comprehension.

The domain of science is one of causal explanations. Purpose, as such, lies outside of this realm, teleology must find its proper scope elsewhere. The moon was not hung aloft in the heavens to keep aur gas bills down, neither does blood clot to prevent a man from bleeding to death. The formation of the clot may be the saving factor, but its formation and the result of a definite series of genetically related processes or steps, the abscece of any one of which precludes the possibility of success, the presence of them all is tantamount to its completion. So again, bacteria, per se, are not the cause of disease, but rather are they but a single link in a long concatenation of causally connected events which include such other links as hereditary background, environment, age, sex, mental attitude, previous state of health and the variable factors such as type, morphology, mass, and virulence of the bacteria themselves.

What is disease? It may be considered as the reflection of a pathological process or lesion upon the organism as a whole. What is a pathological cal lesion? It may be defined as a morphological expression of disproportion of values between stimuli and living cells. All living processes may be considered as a resultant of the interplay between various stimuli and the response of living tissue to these stimuli. If the stimulation is of short duration and of mild intensity and the activated tissue returns quickly to a state of equilibrium, - then the process may be considered as physiological.

If on the other hand the stimuli are of great intensity and prolonged in time, then the result may usually be considered as pathological. To state this in another way - irritants are environmental factors which are responsible for the emancipation of organismic potentialities. The degree of disporportion between the stimulating effect of an irritant and the response on the part of the organism determines physiology or pathology. A cloth dipped in water heated to 55°C and applied to a part causes a physiological increase in activity of a part with a pleasing effect and a rapid return to its previous state when the mild irritant is removed. Increase the temperature of the water to 100°C and it stimulates just a bit too much, and on removal there is no rapid return to the status quo ante because actual damage has been done to the tissue and this "burn" is pathological.

As beginning pathologists let us take a part of our early guidance from that great pathologist, Virchow, who said many years ago:

- (1) All knowledge of disease must be based upon objective, anatomical experience.
- (2) Conclusions as to the nature of disease must be based on this experience and be made strictly according to natural laws of cause and effect."

There may be many exceptions to these rules at the present time but they still may serve as a sure foundation for accurate, restrained, scientific thinking in pathology. At times, perchance we shall leave our special field and induldge in theorizing and interpretation and where facts fail us take the perfectly legitimate heuristic, somewhat circuitous route to truth, but when so doing we knowing ly leave the sphere of pure science and enter the domain of phylosophy and metaphysics.

with these few introductory remarks let us begin our work with a consideration of some of the changes that take place in tissues.

### Morphological Fluidity

The basic factor in growth; characteristic of higher forms; ante eates birth, postdates death.

### Differentiation - a function of environment

- 1. Mitotic at rest
- 2. Amitotic inactive cells

### Growth Requisi tes

- 1. Transudation increased nutritive supply
- 2. Assimilation ability of the tissue to use it; depends on the permeability of the cell
- 3. Procreation formation of new protoplasm

#### Protomeres

Smallest living units which have all of the characteristics of living protoplasm. These increase in geometrical progression from generation, the nuclear plasma material, however, remaining in constant proportion.

### Cloudy Swelling

When on the positive side it is the first step in the process of greater assimilation and increase in protoplasmic content.

### Hypertrophy

Increase in protoplasmic content and structures already present

### Hyperplasia

Numerical increase in cell elements and protoplasmic content. Both content and fun ction are constant in type

#### Regeneration

An inherent characteristic of living matter. Young cells form an ANLAGEN whose direction of differentiation is then a function of environment. There is always a tendency bto overproduce.

Connective Tissue - from fibroblasts

Cartilage - from perichondroblasts or fibroblasts

Bone - from periosteum, endosteum or chondroclasts(?)

Vessels - endothelial buds from preexisting vessels

Blood - reappearance of myeloid foci of embryonic type in bone marrow, liver and speen

Muscles - hypertrophy rather than hyperplasia the rule

Neuroglia - from new formes astrocytes

Nerve - by extension from the proximal part of the fiber only Ganglion Cell - no true regeneration when totally destroyed Epithelial Cells

Lining - Parenchymal - no true regeneration if integrity of the architectural plan has been disturbed

## Abnormal Regeneration

Abortive or pathological, the result of destruction of normal ax skeletal structure by trauma or disease

Scar Tissue - substitution of lower tissue in injury

### Regression Movements

- I. Atrophy quantitative regressive movement in tissue
  - 1. Reducesd in size
  - 2. Patchy reduction in protoplasm
  - 3. Apparent excess of nuclear structures
  - 4. Pigment collection
  - 5. Reduced oxidation
  - 6. Reduced function
  - 7. Hydopsical dissolution

#### Causes

- 1. Interruption of nerve cell control
- 2. Insufficiency of self regulation
- 3. Nutritive interference

### II. Cloudy Swelling

Granular degeneration of cell protoplasm in form of precipitated suspensoids. First stage of degeneration when on the negative side. When severe the nuclei may undergoe 1. Pyknosis, 2. Karryorrhexis and 3. Chromatolysis

## III. Fatty Changes

- 1.Infiltration extracellular collection s of large fat cells as the result of nutritive disturbances in circulatory stasis
- 2. Phanerosis intracellular disintegration of cellular protoplasm as the result of toxic activity
- 3. Lypaemia excess fat in the blood stream, seen in pregnancy, starvation, acidosis, anaesthesia and alcoholism
- 4. Adipocere waxy transformation of dead bodiesin which splitting and degenerating fat derivative replace the muscles

### IV. Hyaline Transformation

Waxy, smooth, glistening, faintly blueish pink staining material seen most frequently in the intimal lining of the blood wessels, and in the muscles in typhoid fever, trichinosis, icterous neonatorum, snake bite, ect.

### V. Amyloid Substitution

Bacon like hyaloid protein degeneration product seen in chronic wasting and purulent processes like Tbc, syphilis, osteomyelitis ect. giving staining reactions similar to starch but which is thought to be a mixture of proteid substance and chondroitin sulphuric acid.

### VI. Mucoid Substitution

Drowning and disintegration of epithelial mucoid cells in their own secretions; coagulates in strings and stains basically

### VII. Colloid Degeneration

Like the others a purely descriptive term referring to substances which look like that substance seen in the thyroid gland. A desquamation of secretory cells due to retention of jelly like product which coagulates in discs and stains pink with acid dyes

### VIII. Carbohydrate Changes

Glycogen content of organs is always in inverse proportion to fat.

- 1. Diabetes Mellitus upset ibn COH metabolism
- 2. Von Gierke's Disease excessive storage of glycogen

#### IX. Protein Changes

Uric acisd the result of breakdown of nucleoproteins

OH cartilages 3. Arthritis

quanine - adenine - highoganthing - tanthine - unic acid

#### Calcium

Normal - 10 mgrms. % in blood, maintained by the activity of the parathyroid glands

Two types

- 1. Indeffusible firmly bound in such tissues as the bones
- 2. Diffusibe
  - a. Unionized playing very little part in the active metabolism of the body
  - b. Ionized the amount in ionic form depends on the carbonic acid tension; when it is reduced the equation goes from left to right and the insoluble tricalcium phosphste is reprecipitated.

 $Ga_{3}(PO_{4})_{2} + 2II_{2}CO_{3} \leftarrow 2CaHPO_{4} + Ca(HOO_{3})_{2} \leftarrow 2Ca^{+} + 2HPO_{4} + Ca^{+} + 2HOO_{3}$ 

Funtion

1. Blood Clotting

Prothrombin - Cephalin - Ga -- Thrombin Thrombin - Fibrinogen -- Fibrin

- 2. Increases contraction of heart muscle
- 3. Direct relation ship to nervous irritability
- 4. Formation of bones
- 5. Balance in Hydogen ion maintainance

Causes of Increase in Galcium

- 1. Halisteresis withdrawal of Ja. from bones as seen in ostemalacia. Calcification follows in the acid juices of such tissues as the stomach and kidney in the presence of alkaline tissue juices
- 2. Parathyroid underactivity in case of tumor displacement of a great deal of the tissue
- 3. Paget's Disease of Bones classification rather obscure at the moment but there is increase in Ca.
- 4. Hyperostosis Frontalis Interna Surg., Gyn., & Obs. 61-353-35

Decrease in Calcium

- 1. Parathyroid over activity
- 2. Alkalaemia
  - a. Gatrointestinal loss of HCl by vomiting
  - b. Hyperphoea blowing of of Co.
  - c. Alkalie ingestion excess NaOH
- 3. Rickets in complete absorption from 0. I. tract
- 4. Nephritis incomplete riddance?

# Calcification

1. Always in degenerated, necrotic, hyaline tissue such as arterial walls in hypertension, atherosclerotic plaques, avascular tumors, scar tissue, abscesses, Tbc. nodes,& exudates, cysts, incrusted parasites etc.

Why Calcification ?

- 1. Physical deposition theory
- 2. Patty acids form insoluble soaps
- 3. Supersaturation maintained by high CO tension
- 4. Necrosis and hyaline metamorphosis

Why in bone at all?

Growing bone contains an enzyme capable of splitting hexose phosphate into hexose & inorganic phosphate.

#### Concretions

- A. Nephrolithiasis B. Cholelithiasis
- C. Pancrestic lithiasis

avascular tumoro, rear tissue, abrurses, The nodes & emolates, ryets, farantes (trichineelis) Why calabiation (2) Physical defeation inslugted (2) Lorthy across to form soops. (3) Luper saturation maintained by high Elle tension (41 Menous + hyrline mela mophoció Why kalcification in love at all Growing love contains our engypore corpable af extitting heyose floorphate into heroes & in. organie phosphate pft. Caz (PO4/2 85% bone. Concretions:= Madney Stones - Nephrolithasis, 5 White Jan Jan 1985 - 12 99 april 1985 Whenever J. J. M. A. 104 12 99 april 1985 Greenental production see could be see could Oxound Ercesins Con Ox over Parathyaid or resilend enters Ech feelulas Wie and engotate in animals i Vitamin A defecting Infection & wear shlitters strep slaph KB Polin Insurtation in breasure of

Types Ca POs E. EO2 Estric acid.

(2) Stall Blacker (1) Cholesterof - pure (2) Regment - pure (3) Infection

Thereis Were Gray and Path 17-1-34

(1) Chickoff 1924 - Flightless electricity + stores

(2) Confirmed 1933 - Welhie - blood dile abole topinhe

(3) Nounger - 1892 - discintegration of effet believe of 6B

(4) Elmon + Draham 1932 - suffert Nannye - leaccount for

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In Silving strain African and or flye, abromation the site rollecte. Waring this found there may be infettration of chotestered from hypercholesterelated Agreed and a currence in the amount of the alkali scholate which we responsible for eleming. We feet in the four of an environment with Addated in the this was a fort the when it of inflation a decrease we had a . may result from either or loth of the following (4) (I change in the DH of the till from alkalins to the auch converting the alkali walt te Ale medhete glyrochobi acid which is neither an emiterfying agent for fortror a frefiligery agent for cholesteros (or) 11 a physiologic change in the wall of the gall bladeour which allows resoften of the alberti cholades. The disappearance of alkali cholate, either by conversion to gly cochohi acced or he resorption courses fift of cholesterot the excess cholesterol courses for around the fort chofilets which tend collects around the fort chofilets which tend to coalesce as the cholate is grandwally removed, then the fort acts as a solvent which is responsible for the quanth of interlacing crystals.